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Prognostic Significance of Mucinous Carcinoma of Colon and Rectum: A Prospective Case-Control Study

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Background and Objectives: The clinical meaning of mucinous type of colonic and rectal carcinoma is still controversial. We used clinicopathological and follow-up data prospectively recorded for our series of colon and rectum cancer to compare 2 matched groups of mucinous and nonmucinous cancer patients.

Methods: Two-hundred-forty-eight patients operated for colon and rectum cancer between January 1986 and January 1997 were considered. Thirty-six patients showed mucinous pattern on histologic examination but only 29 (11.7%) had more than 50% of mucin-secreting acini and could be classified as mucinous type. The 29 mucinous cancer patients were compared with 212 nonmucinous cancer patients to evaluate differences in epidemiological and clinical features. A control group from the nonmucinous patients was sorted by matching for age, sex, location, and Dukes stage.

Results: In the case-control groups, survival was better for nonmucinous than for mucinous tumours. Many of the epidemiological findings already observed for mucinous carcinoma were also confirmed.

Conclusions: The existence of prognostic, clinical, and epidemiological differences between mucinous and nonmucinous colorectal carcinoma, together with the preliminary reports about their difference as to genetic features, could support the hypothesis that mucinous type is a distinct biological entity.

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KEY WORDS: **colorectal carcinoma; mucinous adenocarcinoma; survival rate**

INTRODUCTION

Mucinous adenocarcinoma is one of the histological types of colorectal cancer, described more than 70 years ago [1]. It is defined as a tumour having more than 50% of its body showing mucinous pattern on histological examination [2], with a large amount of extracellular mucin produced by secreting acini. In addition, different specific clinical features have been described for mucinous carcinoma: It affects younger patients, it is more frequent in the proximal part of the colon, and it usually has a more advanced stage at presentation [3,4].

Despite mucinous carcinoma being a well-defined histological entity and showing some definite clinical features, its prognostic significance is still controversial. While a poor prognosis was reported by some studies [5,6], other studies failed to show a correlation with prognosis at all [7] or found a prognostic significance only for some classes of patients [8].

Usually studies on mucinous carcinoma have been

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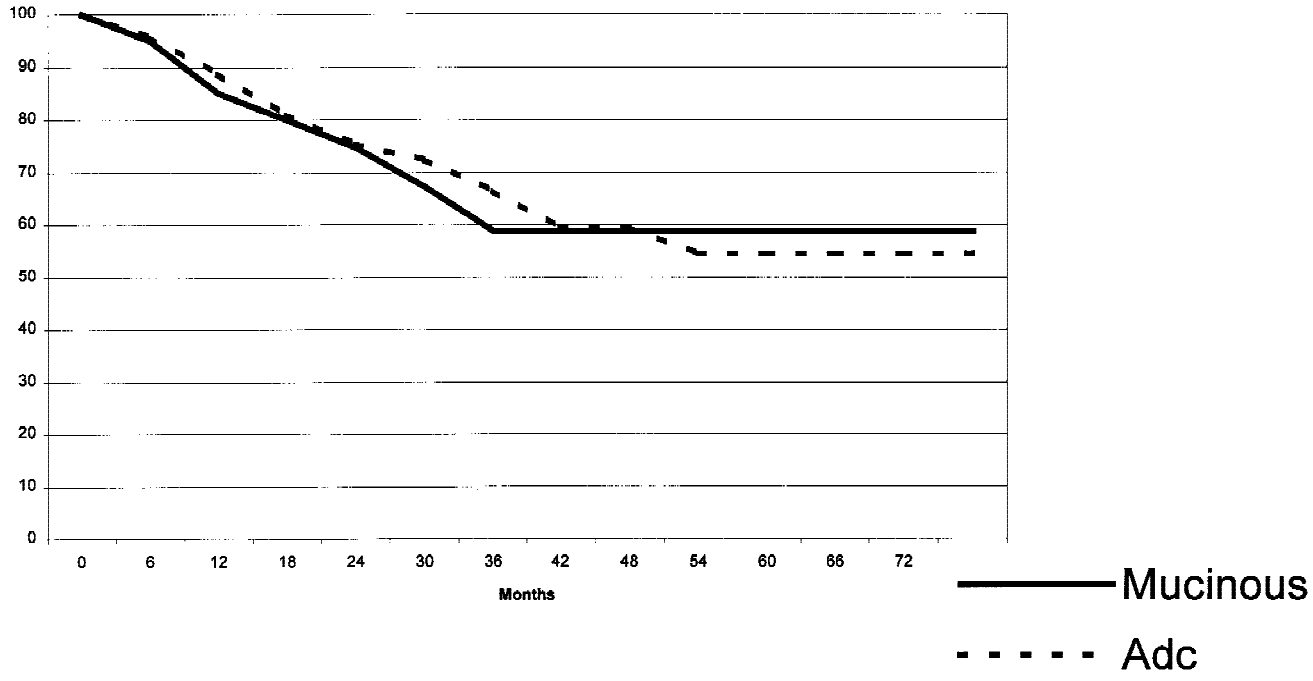

Fig. 1. Compared survival for 29 patients with mucinous tumour (cases) and 58 patients with nonmucinous tumour (controls), matched for age, sex, and Dukes stage.

based on a retrospective review of clinical series, and they tend to compare nonmatched groups of patients.

To avoid the possible bias introduced by a retrospective, nonmatched study, we evaluated the prognostic significance of mucinous carcinoma by comparing 2 groups of mucinous and nonmucinous colorectal cancer patients, matched for other known prognostic factors. We also compared mucinous and non mucinous tumours for their epidemiological and clinical features. All clinicopathological and follow-up data were prospectively recorded.

MATERIALS AND METHODS

Two-hundred-forty-eight patients operated for colon and rectum cancer between January 1986 and January 1997 were considered. Clinicopathological and follow-up data for these patients have been prospectively recorded in an electronic file and in a coded format. Thirty-six patients showed mucinous pattern on histologic examination but only 29 (11.7%) had more than 50% of mucin-secreting acini and could be classified as mucinous type. One case out of the remaining seven was classified as signet ring cell carcinoma.

The 29 mucinous cancer patients were compared with the 212 nonmucinous cancer patients to evaluate differences in epidemiological and clinical features. Then a control group from the nonmucinous patients was sorted by matching for age, sex, location of tumour, and Dukes stage. Two control patients were selected for each case. None of the cases or controls had inflammatory bowel disease. Survival was computed for the case-control groups.

TABLE I. Three-Year Survival for the Case-Control Groups: Overall and Stratified by Dukes Stage[a]

	Mucinous (29 cases)	Nonmucinous (58 controls)
Overall	58.8%	66.3%
Dukes B1-2	87.5%	88.9%
Dukes C1-2	48.5%	69.1%

[a]29 patients with mucinous tumour vs. 58 patients with nonmucinous tumours, matched for age, sex, and Dukes stage.

The mean follow-up time was 37 ± 27 months for nonmucinous (median: 29) and 33 ± 22 (median: 34.5) for mucinous tumours.

Two-tailed *t*-test and χ^2 were used to evaluate differences in means and frequencies, and Kaplan-Meier analysis was performed to evaluate difference in survival. Statistical analysis was performed by SPSS package for Windows.

RESULTS

In the case-control groups, survival was better for nonmucinous than for mucinous tumours (Fig. 1). The difference was mainly explained by survival of Dukes C stages, which was worse for mucinous cancer patients (Table I, Fig. 2). These differences did not reach statistical significance.

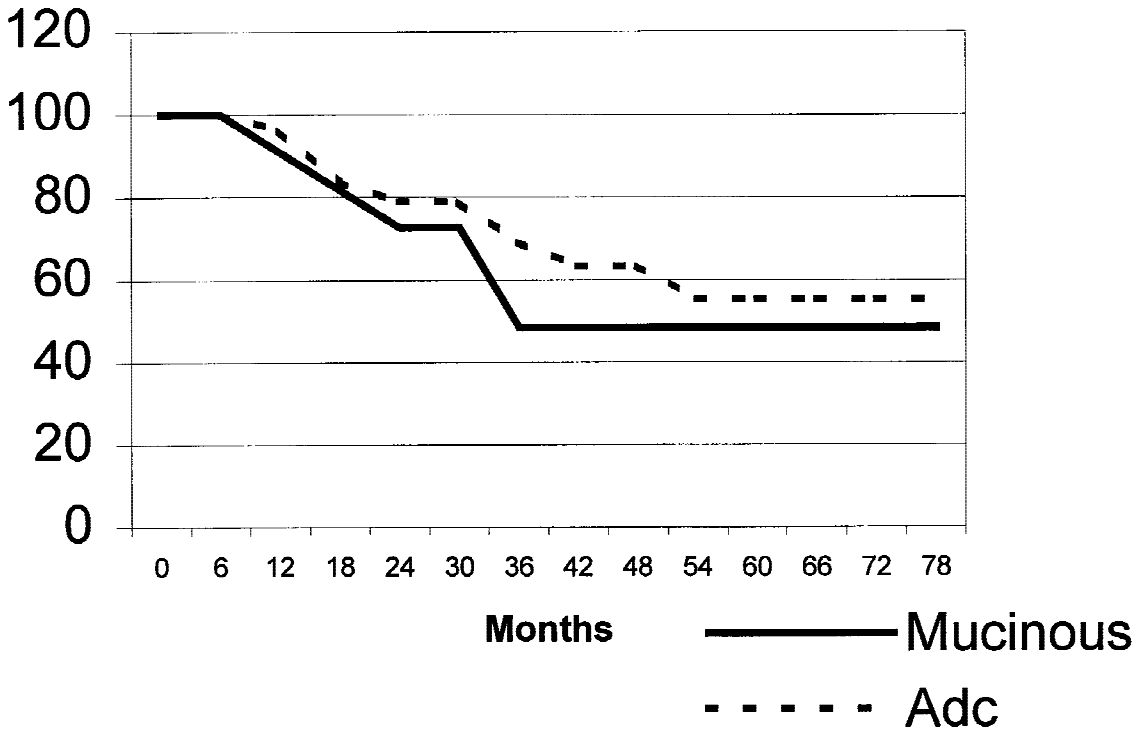

Fig. 2. Compared survival for Dukes C stage patients (15 cases and 30 controls).

There was not a significant difference in survival between colon and rectum location. Similarly, there was no difference as to the pattern of recurrence, with just 3 nonmucinous rectum cancers having pelvic recurrence, 1 mucinous right colon cancer having peritoneal spread, and 22 patients having hepatic metastases (Table II).

In the whole clinical series, the distribution for sex and age of patients with mucinous carcinoma was similar to that of nonmucinous carcinoma patients.

The distribution for location showed an increased incidence of mucinous cancers in the right colon both in absolute number and in proportion with the overall incidence for every section. Mucinous carcinoma constituted 30.5% (11/36) of all the cancers of the cecum and ascending colon.

The stage at the diagnosis showed a little difference, with a higher proportion of more advanced stages for the mucinous carcinoma, even if a significant level was not reached (Table III).

This difference was mainly caused by the pattern of distribution of staging for every location and for every group, with mucinous rectum cancers having a more advanced stage at diagnosis (Table IV).

DISCUSSION

Even though mucinous carcinoma of colon and rectum is a well-recognised entity, its prognostic meaning is still controversial. Actually, various clinical studies assessed survival for patients with mucinous carcinoma with different results. Many of them compared groups of patients who were not matched for stage and location [4,5,8,9] and this could be misleading, since variations in survival could be related to differences in tumour location or stage at presentation rather than being specifically dependent on histological type [10].

Only 2 studies compared matched groups of patients. While Symonds and Vickery [6] observed that mucinous cancers were associated with a significantly lower 5-year survival (34% vs. 53%), Connelly et al. [11] noted no overall differences in survival in a selected group of stage B and C carcinomas (64% each).

In the first study, the difference in survival was mainly related to the rectal locations, which showed a much worse prognosis than the colonic ones. Since patients in this study were operated between 1955 and 1959, the authors considered the possibility of explaining this difference as an outcome of surgical technique, which by that time was more advanced for colon than for rectum.

Our study showed a clear difference in survival: Patients with mucinous carcinoma had a worse prognosis than patients affected by nonmucinous carcinoma, matched for age, sex, location of tumour, and Dukes stage. Difference in survival was mainly related with C stages, without differences in the pattern of recurrence.

Our clinical results are also consistent with the finding of histological features suggestive of a more aggressive behaviour for mucinous carcinoma [12].

Our study confirms the most common clinical findings

TABLE II. Patterns of Recurrences in Case and Control Groups

	Mucinous (29 cases)	Nonmucinous (58 controls)
Local recurrence	0	3
Epatic metastases	7	15
Peritoneal spread	1	0
Death within 36 months	7	11*
Alive with recurrence	1	3

*One more patient died at the 42nd month.

TABLE III. Distribution of Epidemiological and Clinical Features in the Whole Series

	Mucinous: 29 cases (%)	Nonmucinous: 212 cases[a] (%)
Sex (%)[b]	M:51.7 F:48.3	M:53.3 F:46.7
Age (mean s.d.)[b]	61.4 ± 11.1 (min:43; max:83)	64.7 ± 10.5 (min:39; max:91)
Location[c]		
Cecum, ascending	11 (38)	25 (11.8)
C. transverse, descending, sigmoid	8 (27.5)	91 (43)
Rectum	9 (31)	94 (44.3)
Sinchronous asc. + desc.	1 (3.5)	2 (0.9)
Dukes[b] (mod. Astler-Coller)		
A	0	21 (9.9)
B1	5 (17.2)	44 (20.8)
B2	6 (20.7)	55 (25.9)
C1	3 (10.3)	21 (9.9)
C2	12 (41.4)	45 (21.3)
D	3 (10.4)	26 (12.2)

[a]Controls were selected and matched.
[b]Not significant.
[c]$P < 0.002$.

TABLE IV. Stage at Presentation for Mucinous Carcinoma

	Dukes B1-2	Dukes C1-2	Dukes D
Cecum, ascending c.	6	4	1
Transverse, descending c.	0	0	1
Sigmoid	3	4	0
Rectum	1	7	1
Sinchronous	1	0	0

for mucinous carcinoma. The incidence of mucinous type in different studies ranges between 8% and 19%, and in our series mucinous type accounted for 11.7% of all colorectal cancers.

Studies investigating the incidence of colon and rectum cancer in young people showed a higher proportion of mucinous carcinoma [3]. This feature was confirmed by the data from the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute. Since the incidence of colorectal carcinoma in the younger age group is very low, the relatively high frequency of mucinous carcinoma is probably just a reflection of this low overall incidence and of the fact that a young person is more likely to have a mucinous type carcinoma [13]. The age distribution of our group of patients did not show any difference between mucinous and nonmucinous carcinoma. This finding confirms that as soon as the incidence of colorectal carcinoma increases with age, the overall age distribution for mucinous type overlaps the one of adenocarcinoma.

Finally, our data also confirm the higher incidence of mucinous carcinoma in the right sections of the colon.

It is worthwhile noting that despite this fact and although the incidence of carcinoma of the right colon has been increasing the last 30 years [13,14], the incidence of mucinous carcinoma does not show an increasing trend. These observations could support the hypothesis that mucinous carcinoma is a separate biological entity, with a fixed incidence that seems to be independent from the epidemiological evolution of colorectal nonmucinous adenocarcinoma.

Recent acquisitions of molecular biology showed particular features of mucinous carcinoma with respect to nonmucinous type: The expression of p53 protein is lower [15, 16], and DNA replication errors, expressed as microsatellite instability, are more frequent [17]. When ploidy was determined, a higher index of diploidy was found than for nonmucinous carcinoma [16,18].

These findings could suggest a different molecular basis than the one implied in adenomacarcinoma sequence. The genetic mechanism could be similar to that identified for hereditary nonpolyposis colorectal cancer (HNPCC), which is indeed more often of mucinous type [19].

CONCLUSIONS

The existence of prognostic, clinical, and epidemiological differences between mucinous and nonmucinous colorectal carcinoma, together with the preliminary reports about their difference as to genetic features, could support the hypothesis that mucinous type is a distinct biological entity.

More studies are needed about the therapeutic implications of this assumption, mainly to understand if recent advancements in adjuvant therapies fully apply to this histologic type too.

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